

(FILE 'HOME' ENTERED AT 10:24:40 ON 24 MAY 2002)

*Bioscience*

INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL, EMBASE, ESBIODBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, ...' ENTERED AT 10:27:38 ON 24 MAY 2002

SEA (HIN47 OR HTRA) AND INFLUENZAE

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 1 FILE ADISINSIGHT  
 15 FILE BIOSIS  
 1 FILE BIOTECHNO  
 17 FILE CAPLUS  
 1 FILE DDFU  
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 17 FILE IFIPAT  
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 8 FILE NLDB  
 1 FILE PASCAL  
 1 FILE PHIN  
 1 FILE SCISEARCH  
 8 FILE TOXCENTER  
 47 FILE USPATFULL

L1 QUE (HIN47 OR HTRA) AND INFLUENZAE

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 FILE 'CAPLUS, BIOSIS, DGENE, TOXCENTER' ENTERED AT 10:33:25 ON 24 MAY 2002

L2 86 S (HIN47 OR HTRA) AND INFLUENZAE  
 L3 40 S L2 AND NON-PROTEOLYTIC  
 L4 697575 S L2 AND RECOMBINANT OR VECTOR OR PLASMID  
 L5 49 S L2 AND (RECOMBINANT OR VECTOR OR PLASMID)  
 L6 29 S L3 AND L5  
 L7 20983 S OTITIS WITH MEDIA  
 L8 20998 S OTITIS (S) MEDIA  
 L9 20980 S OTITIS (A) MEDIA  
 L10 45182 S HAEMOPHILUS (S) INFLUENZ##  
 L11 2143 S L9 AND L10

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FILE 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGUPDATES, ...' ENTERED AT 10:45:43 ON 24 MAY 2002

L12 75613 S OTITIS (A) MEDIA  
 L13 115360 S HAEMOPHILUS (S) INFLUENZ##  
 L14 7913 S L12 AND L13  
 L15 14 S L14 AND (NON-PROTEOLYTIC OR NON!PROTEOLYTIC)  
 L16 8783 S L12 AND INFLUENZAE  
 L17 529 S (HIN47 OR HTRA) AND (VECTOR OR PLASMID)  
 L18 34 S L16 AND L17  
 L19 29 DUPLICATE REMOVE L18 (5 DUPLICATES REMOVED)

FILE 'MEDLINE, BIOSIS, BIOTECHABS' ENTERED AT 11:21:01 ON 24 MAY 2002

L20 18 S (HIN47 OR HTRA) AND (HAEMOPHILUS (S) INFLUENZ##)

L19 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2002 ACS

AN 1996:294844 CAPLUS

DN 124:334871

TI Cloning and expression of *Haemophilus influenzae* **hin47** gene mutants, and **Hin47** analogs with reduced protease activity for use in diagnosis and as vaccines

IN Loosmore, Sheena M.; Yang, Yan-Ping; Chong, Pele; Oomen, Raymond P.; Klein, Michel H.

PA Connaught Laboratories Limited, Can.

SO PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9603506	A2	19960208	WO 1995-CA434	19950721
	WO 9603506	A3	19960307		
	W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ			
	RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 5506139	A	19960409	US 1994-278091	19940721
	US 5939297	A	19990817	US 1994-296149	19940826
	US 5869302	A	19990209	US 1995-487167	19950607
	AU 9533376	A1	19960222	AU 1995-33376	19950721
	AU 687619	B2	19980226		
	EP 729513	A1	19960904	EP 1995-929690	19950721
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE			
	BR 9506272	A	19970812	BR 1995-6272	19950721
	JP 11509401	T2	19990824	JP 1995-505329	19950721
	US 5981503	A	19991109	US 1996-615271	19960620
	US 5962430	A	19991005	US 1997-801499	19970218
PRAI	US 1994-278091	A	19940721		
	US 1994-296149	A	19940826		
	US 1995-487167	A	19950607		
	US 1995-482816	A3	19950607		
	WO 1995-CA434	W	19950721		
AB	The invention concerns isolated and purified analogs of <i>Haemophilus influenza</i> <b>Hin47</b> protein with decreased protease activity (of less than 10 % of that of the natural protein) but preferably retaining substantially the same immunogenic properties as natural <b>Hin47</b> . Preferred analogs have mutations at Ser197, His91 and/or Asp121 positions and are possibly used as chimeric proteins with other immunogenic mols. Also disclosed are nucleic acids encoding said analogs, recombinant <b>plasmids</b> and transformed host cells contg. said modified genes, immunogenic compns. contg. <b>Hin47</b> analogs or their nucleic acid and their use for prophylactic, vaccine or diagnostic purposes. Ala-197 <b>Hin47</b> protease was produced with recombinant <i>E. coli</i> . This analog had reduced proteolytic activity and immunogenicity comparable to the wild type protease. It was tested in the infant rat model of bacteremia and in the active immunization chinchilla model of <b>otitis media</b>				

L19 ANSWER 29 OF 29 USPATFULL

AN 96:29469 USPATFULL

TI Analog of *haemophilus* **Hin47** with reduced protease activity

IN Loosmore, Sheena M., Aurora, Canada

Yang, Yan-Ping, Willowdale, Canada  
Chong, Pele, Richmond Hill, Canada  
Oomen, Raymond P., Tottenham, Canada  
Klein, Michel H., Willowdale, Canada  
PA Connaught Laboratories Limited, Willowdale, Canada (non-U.S.  
corporation)  
PI US 5506139 19960409  
AI US 1994-278091 19940721 (8)  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Hendricks, Keith  
D.  
LREP Sim & McBurney  
CLMN Number of Claims: 26  
ECL Exemplary Claim: 1  
DRWN 23 Drawing Figure(s); 23 Drawing Page(s)  
LN.CNT 1511

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An isolated and purified analog of *Haemophilus influenzae*  
**Hin47** protein has a decreased protease activity which is less  
than about 10% of that of natural **Hin47** protein and preferably  
substantially the same immunogenic properties as natural **Hin47**  
protein. An isolated and purified nucleic acid molecule encoding the  
**Hin47** analog may be provided in a recombinant **plasmid**  
which may be introduced into a cell which is grown to produce the  
**Hin47** analog. Immunogenic compositions comprising the  
**Hin47** analog and the encoding nucleic acid may be formulated as  
vaccines for in vivo administration to a host, including a human, to  
confer protection against diseases caused by a bacterial pathogen,  
including *Haemophilus* species, such as *Haemophilus influenzae*,  
that produces **Hin47** protein or a protein capable of inducing  
antibodies in the host specifically reactive with **Hin47**  
protein. The **Hin47** analog and the encoding nucleic acid also  
may be employed in diagnostic applications.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L20 ANSWER 7 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 AN 2001:357245 BIOSIS  
 DN PREV200100357245  
 TI Properties of recombinant **HtrA**: An otitis media vaccine candidate antigen from non-typeable **Haemophilus influenzae**.  
 AU Cates, G. A. (1); Yang, Y.-P. (1); Klyushnichenko, V. (1); Oomen, R. (1); Loosmore, S. M. (1)  
 CS (1) Aventis Pasteur, Toronto, ON Canada  
 SO Brown, F.; Corbel, Michael J.; Griffiths, Elwyn. Developments in Biologicals, (2000) Vol. 103, pp. 201-204. Developments in Biologicals. Physico-chemical procedures for the characterization of vaccines. print. Publisher: S. Karger Publishers Inc. 79 Fifth Avenue, New York, NY, 10003, USA.  
 Meeting Info.: Meeting on Physico-Chemical Procedures for the Characterization of Vaccines France December 01-03, 1999  
 ISSN: 1424-6074. ISBN: 3-8055-7101-1 (paper).  
 DT Book; Conference  
 LA English  
 SL English  
 L20 ANSWER 17 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 AN 1997:150674 BIOSIS  
 DN PREV199799449877  
 TI Evidence for PDZ domains in bacteria, yeast, and plants.  
 AU Ponting, Christopher P.  
 CS Fibrinolysis Research Unit, Univ. Oxford, Old Observatory, South Parks Rd., Oxford OX1 3RH UK  
 SO Protein Science, (1997) Vol. 6; No. 2, pp. 464-468.  
 ISSN: 0961-8368.  
 DT Article  
 LA English  
 AB Several dozen signaling proteins are now known to contain 80-100 residue repeats, called PDZ (or DHR or GLGF) domains, several of which interact with the C-terminal tetrapeptide motifs X-Ser/Thr-X-Val-COO- of ion channels and/or receptors. PDZ domains have previously been noted only in mammals, flies, and worms, suggesting that the primordial PDZ domain arose relatively late in eukaryotic evolution. Here, techniques of sequence analysis-including local alignment, profile, and motif database searches-indicate that PDZ domain homologues are present in yeast, plants, and bacteria. It is suggested that two PDZ domains occur in bacterial high-temperature requirement A (**htrA**) and one in tail-specific protease (tsp) homologues, and that a yeast **htrA** homologue contains four PDZ domains. Sequence comparisons suggest that the spread of PDZ domains in these diverse organisms may have occurred via horizontal gene transfer. The known affinity of *Escherichia coli* tsp for C-terminal polypeptides is proposed to be mediated by its PDZ-like domain, in a similar manner to the binding of C-terminal polypeptides by animal PDZ domains.